IN THE CLAIMS:

Please amend claims 1, 4, and 7 and add new claim 30 as follows:

1. (Amended) A method of stimulating ~~an~~ CTL immune response against a tumor antigen in a mammal, the method comprising administering to said mammal said tumor antigen and a lactadherin or a polypeptide comprising a lactadherin amino acid sequence, said polypeptide comprising a functional integrin binding site of lactadherin represented by the RGD motif, in an amount sufficient to elicit a CTL immune response in said mammal.

2-3 (Cancelled).

4. (Amended) The method of claim 1, wherein phagocytosis of said tumor antigens by dendritic cells is stimulated in said mammal.

5. (Original) The method of claim 1, wherein cross-priming of antigens is stimulated in said mammal.

6. (Cancelled)

7. (Amended) The method of ~~any one of~~ claims 1~~-5~~ or 4, wherein said polypeptide is human lactadherin or a polypeptide comprising a functional integrin binding site of human lactadherin.

8-20 (Cancelled).

21. (Previously Amended) The method of claim 1, wherein said lactadherin has the amino acid sequence of SEQ ID NO: 2 or 4 or a part thereof comprising of a functional integrin binding site, said part comprising amino acid residues Arg Gly Asp at position 46-48 of SEQ ID NO: 2 or amino acid residues 87-89 or SEQ ID NO: 4.

22-29 (Cancelled).

30. (New) The method of claim 1 or 4, wherein the tumor antigen is selected from MART-1, MAGE, BAGE, PSA, p53, Rb and Ras.

SPECIFICATION

The specification is amended to conform the description to the sequence listing as specified by the Examiner.

§ 112

All of the objections based on 35 U.S.C. § 112 have been withdrawn by the Examiner.

AMENDMENTS AND NEW CLAIMS

Claim 1 now refers to a method of stimulating a CTL immune response against a tumor antigen in a mammal[...]. Support for this amendment is found on page 1, line 7 of the application.

New claim 30 specifying the nature of the tumor antigen has been added. Support for this amendment is found on page 13, lines 1-4 of the application.

Application reserve their rights to file divisional application(s) at a later stage, to cover any cancelled subject matter.

§102(b)

Claims 1, 4, 5, 7, and 21 stand rejected as allegedly anticipated by U.S. 5,505,955 and by WO 95/15171.

In this Office Action, the Examiner mentions two novel references, i.e. Peterson et al. and Botelho et al. According to the Examiner, the abstracts of the newly cited references indicate

that MUC1 is a tumor antigen (Botelho et al.) and that it is also a component of milk fat globule membrane (Peterson et al.). According to the Examiner, the administration of milk fat globules thus comprises the administration of a tumor antigen.

Applicants wish to draw the Examiner's attention to the fact that Peterson et al. ("Structural and functional aspects of three major glycoproteins of the human milk fat globule membrane") is a document dated from 2001, i.e., after the filing date of the present application, and is therefore unusable to support the rejection made under 35 U.S.C. 102. Furthermore, even when used to complete the disclosure of prior art references, this document fails to anticipate the claimed invention, as discussed below.

Concerning the Examiner's assertion that both references (US 5,505,955 and WO 95/15171) include the administration of the tumor antigen MUC1 itself or via a milk fat globule composition. Applicants wish to stress that none of the cited documents (i.e. Peterson et al., Botelho et al., US 5,505,955 and WO 95/15171) describes their administration in a method of stimulating an immune response against a tumor antigen in a mammal. In particular, WO 95/15171 and US 5,505,955, the HMFG polypeptide is used to treat rotavirus infection through direct interaction with said viruses. The polypeptide or compositions comprising said polypeptide are thus only used for their anti-viral properties. Furthermore, page 17, lines 33-34 of WO 95/15171 indicates that: "The presnet agent [46Kd HMFG molecule] is thus unlikely to elicit toxic, immunological or allergic reactions in treated subjects" (emphasis added).

None of the above-cited references suggests any role of lactadherin on the immune system. None of the above cited references describes a method of stimulating a CTL immune response against a tumor antigen in a mammal, the method comprising administering to said

mammal said tumor antigen and a lactadherin or a polypeptide comprising a lactadherin amino acid sequence.

In this regard, although application WO 95/15171 briefly proposes to use a purified lactadherine "*for vaccinating against neoplastic tumors and cancer*" (page 29, lines 7-9), such brief statement is (i) not documented, (ii) based on the use of purified lactadherin (i.e., without a tumor antigen), and (iii) directed at neutralizing lactadherin itself. Indeed, as mentioned page 55, lines 19-23 of WO 95/15171, lactadherin is overexpressed in some cancer tissues which "*makes it a good target for monoclonal antibody therapy*" (page 55, lines 19-23). This description would thus at best suggest to attempt to neutralize lactadherin in subjects using specific monoclonal antibodies, which is in contrast with the present invention and, based on the teaching of the present invention, is a non-viable approach.

The present application shows for the first time that lactadherin has advantageous properties such as the ability to stimulate dendritic cells, and to deliver antigens to dendritic cells. By stimulating such activity, it is now possible to produce effective CTL responses in patients. The cited references do not contemplate or teach the stimulation of a CTL immune response against a specific tumor antigen, using said tumor antigen, in order to treat or prevent various diseases.

It is thus believed that the invention is novel and inventive over the prior art and that the claims are in condition for allowance.

The Commissioner is authorized to charge **$55.00** Orrick, Herrington & Sutcliffe's Deposit Account No. **150665** for the one-month extension fee and to credit any overpayments to said Deposit Account No. **150665**.

Respectfully submitted,

ORRICK, HERRINGTON & SUTCLIFFE LLP

Dated: October 27, 2003

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